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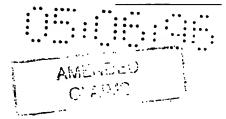
		DOCUMENTS CONS	7					
	Categor		h indication, where a		Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.CI.6)		
2	X	EP 0 341 007 A (P PHARMA (US)) 8 No * page 3, line 18	vember 1989	(1989-11-08)	1,2	A61L25/00 A61L15/44 A61L15/64		
2	х	US 4 006 220 A (G 1 February 1977 (* claims *	OTTLIEB SHELI 1977-02-01)	DON K)	1,2	A61F13/02		
2	х	US 4 061 731 A (G 6 December 1977 (* claims *	0TTLIEB SHELD 1977-12-06)	00N K)	1,2			
2	х	DATABASE WPI Section Ch, Week Derwent Publicatio Class A96, AN 1979 XP002128893 & JP 54 098091 A (2 August 1979 (197 * abstract *	ons Ltd., Lon 9-66949B (UNITIKA LTD)		1,2			
2	X	DATABASE WPI Section Ch, Week 1 Derwent Publicatio Class B04, AN 1980 XP002128894 & SU 700 129 A (KI 30 November 1979 (* abstract *	ns Ltd., Lon -51199C EV HAEMATOLO		1,2	TECHNICAL FIELDS SEARCHED (Int.CI.6) A61L A61F		
2	- 1	EP 0 365 705 A (TS PROBLEMNA LAB KRYOBIOLOGIA) 2 May 1990 (1990-05-02) * claims; examples *			1-9			
2 /		US 4 637 815 A (LEI 20 January 1987 (19 * claims *	987-01-20)	-/	1-9	·		
		The supplementary search repo et of claims valid and available						
e e	THE HACKE			plation of the search		Examiner		
(P04C04)		THE HAGUE	27 Ja	nuary 2000	ESP	INOSA, M		
1303 03.82	X : particu Y : particu docum A : techno	EGORY OF CITED DOCUMENTS ularly relevant if taken alone ularly relevant if combined with another ent of the same category logical background rither disclosure.	to theory or principle underlying the invention E: earlier patent document, but published on, or after the filing date			hed on, or		
ב ב	O : non-written disclosure P : intermediate document			i. member of the same patent family, corresponding document				



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	Category	DOCUMENTS CONSID Citation of document with in of relevant pass:	Relevant	CLASSIFICATION OF TH				
2	Α	WO 93 06855 4 (NOVO	NODDICK AC)	to claim	APPLICATION (Int.CI.6)			
		15 April 1993 (1993	-04-15)					
2	Α	WO 90 13320 A (FERR	OSAN AS)					
		15 November 1990 (1	990-11-15)					
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					TECHNICAL FIELDS SEARCHED (Int.CL6)			
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	set o	supplementary search report has claims valid and available at the	been based on the last start of the search.					
•		HAGUE	Date of completion of the search	Ex	Wriner			
		RY OF CITED DOCUMENTS	27 January 2000	ESPINOS	A, M			
X :	X : particularly relevant 2 4-1			T: theory or principle underlying the invention E: earlier patent document, but published on, after the filling date.				
	document o	the same	D : document cited in the	"	or (
A : technological background O : non-written disclosure P : intermediate document			2. Goodstand dred for othe	2. Goodfield died for other reasons				
			is member of the same patent family, corresponding document					



Claims:

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1. A hemostatic patch adapted for rapidly and without pre-moistening arresting bleeding from a lesion on a parenchymal organ, in the form of a dry sterile storage stable fibrinogen-free flexible sheet of a biodegradable matrix containing a hemostatic agent on one face only thereof, which hemostatic agent comprises an amount of thrombin, optionally bovine thrombin, effective to promote accelerated hemostasis and an amount of epsilon aminocaproic acid effective to inhibit fibrinolysis and to accelerate the activation of the thrombin when the patch is applied to the bleeding lesion;

optionally said patch containing one or more of a source of calcium ions, RGD peptide, RGDS peptide, protamine sulfate and buffer.

- 20 2. A hemostatic patch according to claim 1, wherein the biodegradable matrix is:
 - (a) a foam, optionally an absorbable gelatin foam;
- (b) selected from absorbable gelatin, calcium alginate, calcium/sodium alginate, collagen and oxidized regenerated cellulose.
- 30 3. A hemostatic patch according to claim 1 or claim 2, wherein:
 - (a) the epsilon aminocaproic acid is present in an amount from about $10-100 \, \text{mg/cm}^2$ of the wound-contacting



surface of the matrix, e.g. $60-70\,\mathrm{mg/cm^2}$ of the wound-contacting surface of the matrix; and/or

- (b) the thrombin is present in an amount between 1-5 4 IU/cm² of the wound-contacting surface of the matrix; and/or
- (c) calcium ions are present in an amount equivalent to 25-150 micrograms CaCl₂/cm² of the wound-contacting surface of the matrix.
- 4. A dry sterile storage stable fibrogen-free hemostatic patch comprising a biodegradable matrix containing a hemostasis-promoting amount of thrombin, optionally bovine thrombin, and an amount of a compound which is effective to raise the pH of fluid on a bleeding wound surface onto which the hemostatic patch is applied to a value in the range of 7.0-9.0, e.g. 7.62-8.02, inclusive, and which is thereby effective to accelerate the activation of the thrombin and thus accelerate clot formation at the interface between the wound surface and the hemostatic patch.
- 5. A hemostatic patch according to claim 4, wherein the thrombin-activating compound is epsilon aminocaproic acid.
- 6. A hemostatic patch according to claim 4 or claim 5 and further defined by any specific feature(s) of any one or more of claims 2 and 3.
- A hemostatic patch according to claim 4, wherein the biodegradable matrix is a flexible sheet
 of an absorbable gelatin foam, wherein the patch



optionally contains one or more of a source of RGD peptide, RGDS peptide, protamine sulfate and buffer; wherein epsilon aminocaproic acid is present therein in an amount between 60-70mg/cm² of the wound-contacting surface of the matrix; wherein the thrombin is present therein in an amount between 1-4 IU/cm² of the wound-contacting surface of the matrix; and wherein calcium ions are present in an amount equivalent to between 25-150 micrograms of CaCl₂/CM² of the wound-contacting surface of the matrix.

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- 8. A sterile package containing a hemostatic patch according to any one of claims 1 to 7.
- 9. The use of a dry sterile storage stable fibrinogen-free biodegradable matrix containing a hemostatic agent, which hemostatic agent comprises an amount of thrombin, optionally bovine thrombin, effective to promote accelerated hemostasis and an amount of epsilon aminocaproic acid effective to inhibit fibrinolysis and to accelerate the activation of the thrombin, in the manufacture of a medicament patch.